This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.



FIG. IA(I)

1	GC	ACC	GCG	SCGA	\GC1	TGG	CTC	CTI	'CTG	GGG
84	GGC	:CGC	GAC	ccc	TCI	GAC	CGA	GAT	* CCI	AG GCT
168	CGT GT G	CCC	C TG	GG SCCC	CTC GGA	CGC	GCI TGG	CCC	CG GAT	GAA(
252 1	ACC GGA	GA GTC	CAC	CCCC	TGG GAC	GGG CCC	ACC CGA	: .CTC	TCG CAA	AT GCG
336	T CCT		G GAT		GCT		G ACC	ACC	Ϋ́СХ	CAG
9	P S	T	D E		A		T		s	Q
420	G TTA	TTA	AAG	_	GTT		G GCA		געעע	GAC
37	L	L	K			G		Q	K N	D
504	A G		TAT	C GAT		AAG		G CAA		ATTG
65	R			D		K			H	I
	ama:	G	~- ~						G A	
588	GTG:	AAA!	GAG	CAC	AGG	AAA.	ATA _	TAT	ACC:	ATGA
93	V	K	Ŀ	н	R	K	I	Y	T A	M
	G	С			G	λ	C	,G	C	
672			AGT	GAG.	AAC.	AGG'	O TGT:	CAC	շփփ	GAAG
121	·s·	v	S	E	N	R	C	H	L	E
		Ŀ		•				0		



FIG. 1A(2)

CTGTGTGGCCCTGTGTGTCGGAAAGATGGAGCAAGA

AGCCGC GC TTCTC TCG TCGAGCT TG ACGAC CTTTCGCAGCCAGGAGCACCGTCCCTCCCCGGATTA

GTCGGAA ATGCGC G AAGTAG CC T CT GAGGCCCAGGGCGTCGTGCTTCCGCAGTAGTCAGTC

ACCGCG TTCTCCT C GCCTC C
GAAAACCCCGGATGGTGAGGAGCAGGCAAATGTGCA
M C

G
TATATTGTTCAAATGATCTTCTAGGAGATTTGTTTG
V Y C S N D L L G D L F
V

A T A G CT A G A---TCTACAGGAACTTGGTAGTAGTCAGCAGGAAT
I Y R N L V V V N Q Q E
A S -

TG T C T G C CA

GTGGGAGTGATCAAAAAGGACCTTGTACAAGAGCTTC
G G S D Q K D L V Q E L
L P L A P



FIG. 1A(3)

AG	CCG.	AGC	CCG	AGG	GGC		83	Human	nt
	TG							Mouse	nt
GT	GCG'	TAC	GAG	CGĆ	CCA		167	Human	nt
GG	GCG	AGC	G.	AGA	CC			Mouse	nt
CC	CGT	GAA	GGA	AAC'	TGG		251	Human	
					G			Mouse	nt.
AT	ACC	AAC	ATG!	rcT(GTA		335	Human	
N	${f T}$	N	M	S	V		8	Human	a.a.
٠					·			Mouse	
A	•							Mouse	nt
AG	CCA	rtg	ETT:	r TG	AAG		419	Human	nt
K	P	L	L	L	K		36	Human	a.a.
								Mouse	a.a.
					G			Mouse	nt
	rati			ACT	AAA		503	Human.	nt
Q	Y	I	M	${f T}$	K		64	Human	a.a.
								Mouse	a.a.
	С							Mouse	nt
GC	STGC	CA	\GC1	CTC	rĊT		587	Human	nt
G	¥	P	S	F	S		92	Human	a.a.
								Mouse	a.a.
			\mathbf{T}	С				Mouse	nt
CA	rcg(FACT	CAC	GTI	ACA	-	671	Human	nt
S	S	D	S	G	${f T}$		120	Human	a.a.
-	-							Mouse	
CA								Mouse	nt
AGO	SAAG	SAG	AAA(CTI	CA		755	Human	nt
Q	E	E	K	P	S		148	Human	
P								Mouse	



FIG. 18(1)

		m	~	78.	7.			mc	
756	mam				A				mom
	TCT								
149	S	8				S			5
	٠		D		Ι	٠		L	
	G	G	G	C	C G	G		G	GG
840	GGT	GAA	CGA	CAA	AGA	AAA	CGC	CAC	AAA
177	G	\mathbf{E}	R	Q	R	K	R	H	K
				H				R	$\cdot \mathbf{R}$
	G	C	AGC	GGC	GGC.	ACG.	AGC	A C	AGT
924	ATA	TGT						TGT	GAA
205	ATA' I	C	-		-	•••	-	C	E
	M		S	G	G	T	S	s	S
			G		${f T}$			C	C.
993	GTA	AGT							
	V								
	•					. •			
								_	
	G			C		C			
1077					3 C C			С	
1077	TCA	GAA	GAT!	TAT	AGC	CTT	AGT	C GAA	GAA
1077 256	TCA	GAA	GAT!	TAT	AGC	CTT	AGT	C GAA E	GAA
	TCA	GAA	GAT!	TAT	AGC	CTT	AGT	C GAA	GAA
256	TCA S A	GAA E A	GAT' D C	TAT Y	AGC S	CTT L C	AGT S	C GAA E D	GAA E
256 1161	TCA S A GGG	GAA E A GAG	GAT' D C AGT	TAT Y GAT	AGC S ACA	CTT L C GAT	AGT S T	C GAA E D	GAA E
256 1161	TCA S A	GAA E A GAG	GAT' D C AGT	TAT Y GAT	AGC S ACA	CTT L C GAT	AGT S	C GAA E D	GAA E
256 1161	TCA S A GGG	GAA E A GAG	GAT' D C AGT	TAT Y GAT	AGC S ACA	CTT L C GAT	AGT S T	C GAA E D	GAA E GAA
256 1161	TCA S A GGG	GAA E A GAG	GAT' D C AGT	TAT Y GAT	AGC S ACA	CTT L C GAT	AGT S T	C GAA E D TTT	GAA E GAA
256 1161	TCA S A GGG G	GAA E A GAG E	GAT' D C AGT S	TAT Y GAT D	AGC S ACA T	CTT L C GAT D	AGT S TCA S	C GAA E D TTT	GAA E GAA E
256 1161 284	TCA S A GGG G	GAA E A GAG E	GAT' D C AGT	TAT Y GAT D	AGC S ACA T	CTT L C GAT D	AGT S TCA S	C GAA E D TTT	GAA E GAA E
256 1161 284 1245	TCA S A GGG G	GAA E A GAG E	GAT' D C AGT	TAT Y GAT D	AGC S ACA T	CTT L C GAT D	AGT S TCA S	C GAA E D TTT F	GAA E GAA E A
256 1161 284 1245	TCA S A GGG G	GAA E A GAG E	GAT' D C AGT	TAT Y GAT D	AGC S ACA T CCA	CTT L C GAT D	AGT S TCA S	C GAA E D TTT F	GAA E GAA E A AAC N
256 1161 284 1245	TCA S A GGG G	GAA E A GAG E T CCC	GAT' CAGT	GAT D CTT L	AGC S ACA T CCA	CTT L C GAT D	AGT S TCA S CAT H	C GAA E D TTT F	GAA E GAA E AAC N K



FIG. 18(2)

					. 1	T C						G
ACC!	TCA!	rct:	AGA	AGG	AGA	GCA	TTA	AGT	GAG.	ACA	GAA	GAA
T	S	S	R	R	R	A S	I	S	E	T	E	E
					~				000			G
TCT		A CAT	2 mm		G Cmm						ርጥር.	_
										S		
- .	_	_		J		•	•		P	•		G
									~			•
С		С		С	G	С		Α		С	-	С
AGA:												
	S	S	S	S	E	S	T		\mathbf{T}_{\cdot}	P	S	
S		•						E				H
					${f T}$				С	G		
GAT	CAG	GAT	TCA	GTT							GAA	TTT
D	Q	D	S	\mathbf{v}	S	D	Q	\mathbf{F}_{\cdot}	S	V	\mathbf{E}_{\perp}	F
·G	C	G				G				C		GG
GGA											ጥልጥ	
			-							v		Q
	Ĥ				_							Ŕ
	•											
G			G	٠							G	\mathbf{T}
GAA												TGC
E	D	P	E	I	S	L	A	D	Y	W	K	С
G				÷								•
	·		Δ				C			Δ	С	i
AGA	TGT'			CTT	CGT	GAG	_		CTT	_		
				-						P		
			${f T}$							•	D	
	•											
										G		
AAC												
N	8	T A	δ	Α	E	Ŀ	G	F L	ט	V	צ	ט
		77						ىد				



FIG. 1B (3)

CZ	Ą		G	Ċ	C		Mouse	nt.
AAT	rca(TAE	SAA	ATT	TCT	839	Human	nt
N	S	D .	E	L	S	176	Human	a.a.
	${f T}$				P	•	Mouse	a.a.
		AGO	CG				Mouse	nt
CTG	rgre	TAZ	ATA	AGG	GAG	923	Human	nt
L	C	V	I	R	E	204	Human	a.a.
		E	L				Mouse	a.a.
			•					
A				A			Mouse	nt
CCG	SATO	CTTC	SATO	SCT	GGT	992	Human	nt
P	D	L	D		G	227	Human	
Q				D			Mouse	a.a.
		_		_				•
~		G		G			Mouse	
GAA						1076	Human	
E	V	E	S	L	D	255	Human	
•	•	•					Mouse	a.a.
\sim	7\	C			λ	•	Mouso	n+
	A CTC				A GCA	1160	Mouse	
GTT	ACTO	FTGI	TAT	CAG	GCA	1160	Human	nt
				CAG	GCA A	1160 283	Human Human	nt a.a.
GTT	ACTO	FTGI	TAT	CAG	GCA		Human	nt a.a.
GTT	ACTO	FTGI	TAT	CAG	GCA A		Human Human Mouse	nt a.a. a.a.
GTT2 V	ACT (TG1 V	YATO Y	CAG Q	GCA A T	283	Human Human Mouse Mouse	nt a.a. a.a.
GTT	T T	TGCI	TATO Y	CAG Q SAA	GCA A T ATG	283	Human Human Mouse Mouse Human	nt a.a. a.a. nt nt
GTTZ V C ACTT	ACT (TG1 V	YATO Y	CAG Q	GCA A T	283	Human Human Mouse Mouse Human Human	nt a.a. a.a. nt nt a.a.
GTTZ V C ACTT	T T	TGCI	TATO Y	CAG Q SAA	GCA A T ATG	283	Human Human Mouse Mouse Human	nt a.a. a.a. nt nt a.a.
GTTZ V C ACTT	T T	TGCI	TATO Y	CAG Q SAA	GCA A T ATG	283	Human Human Mouse Mouse Human Human Mouse	nt a.a. a.a. nt nt a.a.
GTTZ V C ACTT	ACTO T TCAT S	TGT V TGCI C	TATO	Q Q GAA E	GCA A T ATG M	283	Human Human Mouse Mouse Human Human	nt a.a. a.a. nt nt a.a. a.a.
GTTA V C ACTT	ACTO T TCAT S	TGT V TGCI C	TATO	Q Q GAA E	GCA A T ATG M	283 1244 311	Human Human Mouse Mouse Human Human Mouse	nt a.a. nt nt a.a. a.a. nt
C ACTT	TCAT S	TGCI C	Y Y AATO N	CAG Q EAA E	GCA A T ATG M T GGG	283 1244 311 1228	Human Human Mouse Mouse Human Human Mouse Mouse Human	nt a.a. nt a.a. nt nt a.a. nt nt
C ACTT	TCAT S	TGCI C	Y Y AATO N	CAG Q EAA E	GCA A T ATG M GGG G	283 1244 311 1228	Human Human Mouse Human Human Mouse Mouse Human Human Human	nt a.a. nt a.a. nt nt a.a. nt nt
C ACTT	TCAT S	Y Y TGCI C VAAC K	Y Y AATO N	CAG Q EAA E	GCA A T ATG M GGG G	283 1244 311 1228	Human Human Mouse Human Human Mouse Mouse Human Human Human Human	nt a.a. nt a.a. nt nt a.a. nt nt
C ACTT T G AAAC	ACTO T CAT S G G	TGT V TGCI C C	AATO N GATI	CAG Q EAA E	GCA A T ATG M T GGG G V A	283 1244 311 1228	Human Human Mouse Human Human Mouse Mouse Human Human Human Human	nt a.a. nt a.a. nt nt a.a. a.a.
GTTA V C ACTT T G AAAC K	ACTO T CAT S G G	TGT V TGCI C C	AATO N GATI	CAG Q EAA E	GCA A T ATG M T GGG G V A	283 1244 311 1228 339	Human Human Mouse Human Human Mouse Mouse Human Human Human Human Human Human Human	nt a.a. nt a.a. nt nt a.a. nt nt nt nt



FIG. IC(1)

			G J	A		С	•	С		G
1413	AAT	GAT	TCC	CAGA	GAG	TCF	TGI	GTI	'GAG	GAA
368	N	D	S	R	E	S	C	V	E	E
			A	K		P		A		
•		A		G		-	: C			G
1494	TCT	CAG	CCA	TCA	ACI	TCI	'AGT	AGC	ATI	'ÀTI
395	S	Q	P	S	T	S	S	S	I	I
										V
	С							C		G
1578	GAA					TCT		TTG	CCC	CTT
423	E	E	S	V	E	S	S	L	P	L
	D							\mathbf{F}	S	
	~	_	•	_	_		_			
1600	T	C			T					T A
1662	GTC									
451	V	H	G	K	T	G	H	L	.M .	A
•			•							S
	•	G		С						G
1746	AGA			_		ΆΤς	እጥጥ	GTG	ርጥ አ	
479	R	Q	P		Q			v	L	T
		~			æ		_	•	~	ŝ
1830	TAAC	CCC	TAG	GAA	TTT	AGA	CAA	CCT	GAA	ATT
1914	TTAC	STA!	TAA	TTG	ACC	TAC	TTT	GGT.	AGT	GGA
1998	ACT									
2082	ATG									
2166	CTC	rgc	CCT	CCC	CGG	GTT	CGC	ACC:	TTA	CTC
2250	TAAT	CTT:	rrr _'	GTA	CTT	TTA	GTA	GAG:	ACA	GGG
2334	CTCC									



FIG. IC(2)

G CAGC G GGCCGA GA GC C TG C AAT---GATGATAAAATTACACAAGCTTCACAATCAC I T Q A D D K S D S \mathbf{E} E Α E T P Τ.

AGC G--- A
TATAGCAGCCAAGAAGATGTGAAAGAGTTTGAAAGGG
Y S S Q E D V K E F E R
S L - K

C A C C G G G AATGCCATTGAACCTTGTGTGATTTGTCAAGGTCGAC N A I E P C V I C Q G R

T C G A A C
TGCTTTACATGTGCAAAGAAGCTAAAGAAAAGGAATA
C F T C A K K L K K R N

C AA C CTCA A A T
TATTTCCCCTAGTTGACCTG---TCTATAAGAGAATT
Y F P
N



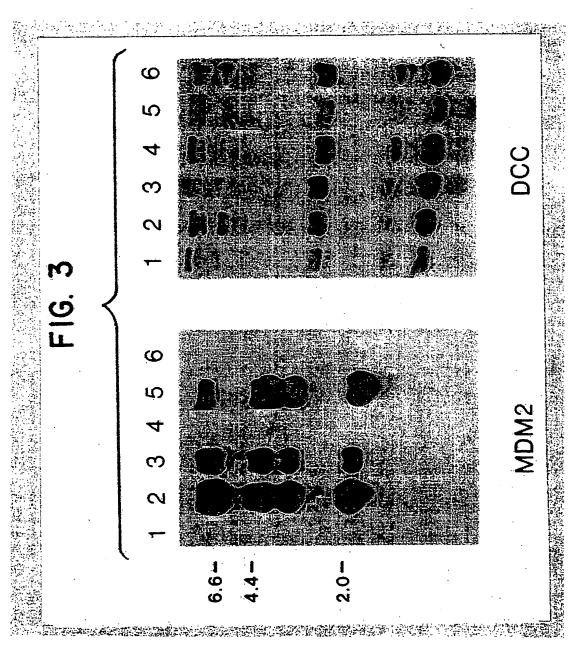
FIG. IC(3)

G G C		Mouse nt
AAGAAAGTGAAGACTAT	1493	Human nt
Q E S E D Y	394	Human a.a.
D		Mouse a.a.
G G GG	•	Mouse nt
G G GC	1577	Human nt
AAGAAACCCAAGACAAA	422	•
E E T Q D K	422	Human a.a.
Н		Mouse a.a.
C		Mouse nt
CTAAAAATGGTTGCATT	1661	Human nt
P K N G C I	450	Human a.a.
		Mouse a.a.
G C		Mouse nt
AGCCCTGCCCAGTATGT	1745	Human nt
K P C P V C	478	Human a.a.
· · · · · · · · · · · · · · · · · · ·		Mouse a.a.
T *		Mouse nt
ATATATTTCTAACTATA	1829	Human nt
	491	Human a.a.
		Mouse a.a.
ACATAGATTTCTTCTCT	1913	Human nt
GCTCATCCTTTACACCA	1997	Human nt
ATGTATATGACATTTAA	2081	Human nt
TCTTGGCTCACTGCAAG	2165	Human nt
CTGCCACCACACCTGGC	2249	Human nt
CCTCGTGATCCGCCCAC	2333	Human nt
COLOGIGATOCGCCCAC	2372	Human nt

F1G. 2

1 2 3		MDM2 + + + P53 MCC	MDM2 Ab p53 Ab1 + p53 Ab2 + Serum
4 5 8		+ + + + + +	* *
7 8 9		+ + + + + + +	* * * *
10 11 12 13 14	MCC / MDM2 - p53 - m	* * * * *	* *
15 16		++	+







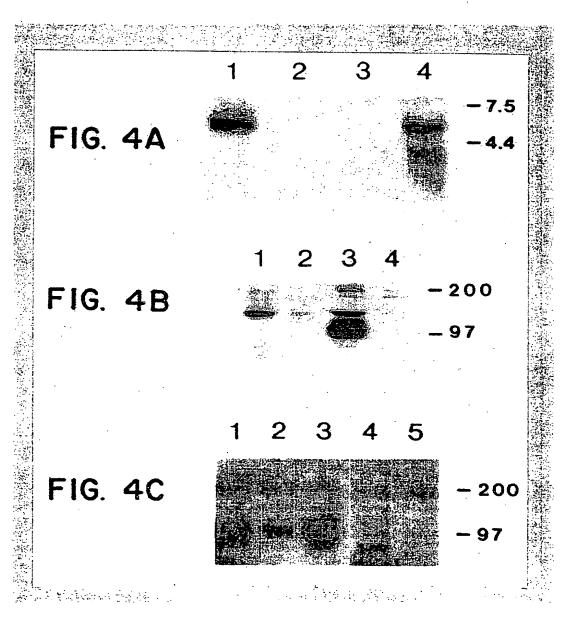
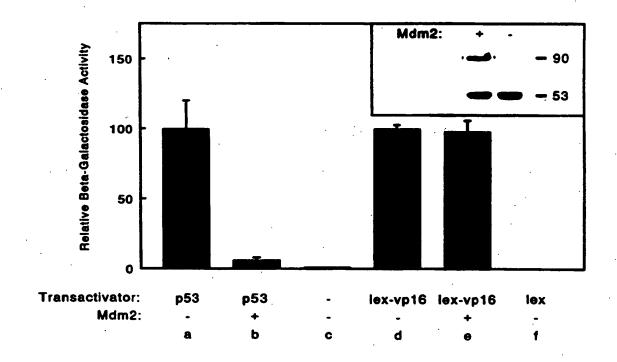
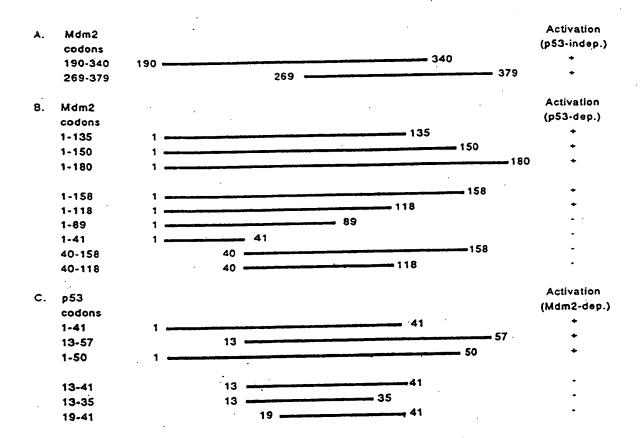




FIG. 5







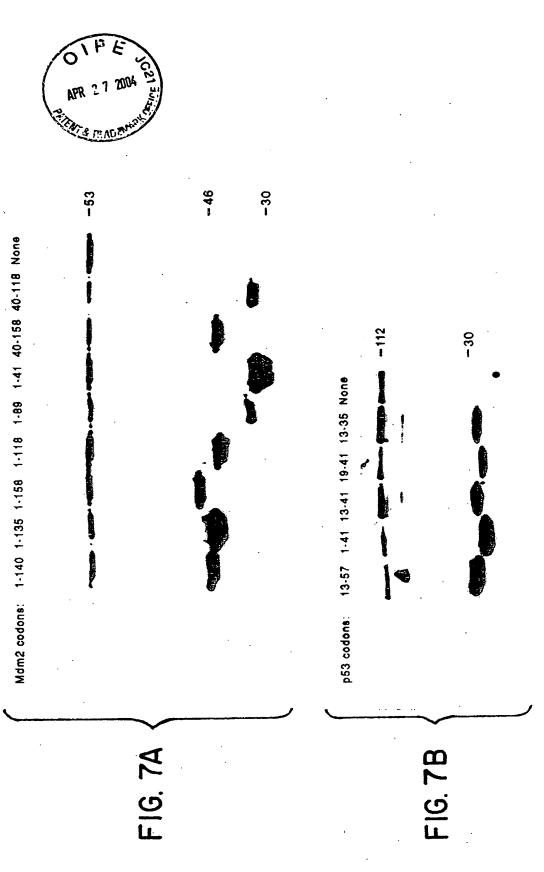
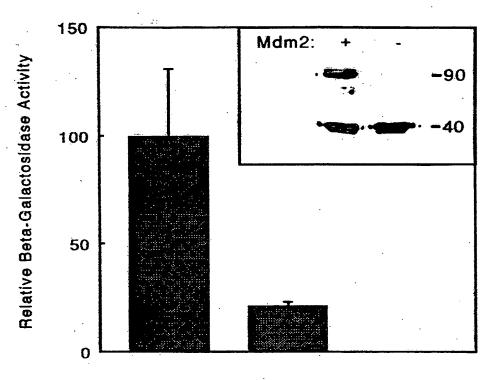




FIG. 8



Transactivator:

Mdm2:

lex-p53

lex-p53

lex

а

b

··C